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PATENT TRADEMARK OFFICE

Docket No.: 1946/1B861-US2

EL767719190US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Andrea Leone-Bay, Sam J. Milstein, Donald J. Sarubbi, and Harry Leipold

Serial No.: Not Yet Assigned — Group Art Unit: Not Yet Assigned

Filed: Concurrently Herewith — Examiner: Not Yet Assigned

For: COMPOUNDS AND COMPOSITIONS FOR DELIVERING ACTIVE AGENTS

PRELIMINARY AMENDMENT

Hon. Commissioner of
Patents and Trademarks
Washington, DC 20231

Sir:

Before examination and calculation of the filing fee, kindly amend the above-identified application as follows:

IN THE SPECIFICATION:

Please amend the specification pursuant to 37 C.F.R. §1.121 as follows:

Replace the paragraph at page 1, lines 11-13, with the following two paragraphs:

CROSS-REFERENCE TO OTHER RELATED APPLICATIONS

The present application is a continuation of U.S. Application Serial No. 08/820,694, filed March 18, 1997, and claims the benefit under 35 U.S.C. §119 of U.S. Provisional Patent Application Serial No. 60/017,902, filed March 29, 1996, both of which are hereby incorporated by reference and made part of the instant disclosure.

Replace the paragraph at page 20, lines 5-20, with the following paragraph:

Biologically or chemically active agents include, but are not limited to, pesticides, pharmacological agents, and therapeutic agents. For example, biologically or chemically active agents suitable for use in the present invention include, but are not limited to, peptides, and particularly small peptides; hormones, and particularly hormones which by themselves do not or only a fraction of the administered dose passes through the gastro-intestinal mucosa and/or are susceptible to chemical cleavage by acids and enzymes in the gastro-intestinal tract; polysaccharides, and particularly mixtures of muco-polysaccharides; carbohydrates; lipids; or any combination thereof. Further examples include, but are not limited to, human growth hormones; bovine growth hormones; growth releasing hormones; interferons; interleukin-1; interleukin-II; insulin; heparin, and particularly low molecular weight heparin; calcitonin; erythropoietin; atrial naturetic factor; antigens; monoclonal antibodies; somatostatin; adrenocorticotropin, gonadotropin releasing hormone; oxytocin; vasopressin; cromolyn sodium (sodium or disodium chromoglycate); vancomycin;

desferrioxamine (DFO); parathyroid hormone; anti-microbials, including, but not limited to anti-fungal agents; or any combination thereof.

IN THE CLAIMS:

Cancel claims 1-19 without prejudice.

Add claims 20-46 reading as follows:

20. A pharmacological composition comprising:

(A) at least one biologically-active agent; and

(B) at least one carrier compound having the formula

2-HO-Ar-CONR^8-R^7-COOH

or a salt thereof

wherein Ar is a substituted phenyl or naphthyl;

R^7 is selected form the group consisting of C_4 to C_{20} alkyl, C_4 to C_{20} alkenyl, phenyl, naphthyl, (C_1 to C_{10} alkyl)phenyl, (C_1 to C_{10} alkenyl)phenyl, (C_1 to C_{10} alkyl)naphthyl, (C_1 to C_{10} alkenyl) naphthyl, phenyl (C_1 to C_{10} alkyl), phenyl (C_1 to C_{10} alkenyl), naphthyl (C_1 to C_{10} alkyl) and naphthyl (C_1 to C_{10} alkenyl);

R^7 is optionally substituted with C_1 to C_4 alkyl, C_1 to C_4 alkenyl, C_1 to C_4 alkoxy, -OH, -SH and -CO_2R^9 or any combination thereof;

R^7 is optionally interrupted by oxygen, nitrogen, sulfur or any combination thereof;

R^8 is selected from the group consisting of hydrogen, C_1 to C_4 alkyl, C_1 to C_4 alkenyl, hydroxy, and C_1 to C_4 alkoxy; and

R^9 is hydrogen, C_1 to C_4 alkyl, or C_1 to C_4 alkenyl;

with the proviso that the compounds are not substituted with an amino group in the position alpha to the acid group.

21. The composition of claim 20, wherein Ar is substituted with at least one of C_1-C_5 alkyl, C_2-C_4 alkenyl, -F, -Cl, -OH, $-SO_2$, -COOH or $-SO_3H$.

22. The composition of claim 21 wherein Ar is a substituted phenyl.

23. The composition of claim 21, wherein Ar is a phenyl substituted with -Cl.

24. The composition of claim 21, wherein Ar is a phenyl substituted with -F.

25. The composition of claim 23, wherein R^7 is selected from the group consisting of C_4 to C_{20} alkyl, (C_1-C_{10} alkyl)phenyl, and phenyl (C_1 to C_{10} alkyl).

26. The composition of claim 23, wherein R^7 is C_4-C_{20} alkyl.

27. The composition of claim 26, wherein R^7 is not substituted or interrupted.

28. The composition of claim 27, wherein R^8 is hydrogen.

29. The composition of claim 20, wherein the biologically active agent comprises at least one peptide, hormone, polysaccharide, mucopolysaccharide, carbohydrate, or lipid.

30. The composition of claim 29, wherein the biologically active agent is a peptide.

31. The composition of claim 29, wherein the biologically active agent is a mucopolysaccharide.

32. The composition according to claim 20, wherein the biologically active agent comprises human growth hormone, bovine growth hormone, growth hormone-releasing hormone, an interferon, interleukin-1, interleukin-II, insulin, heparin, low molecular weight heparin, calcitonin, erythropoietin, atrial naturetic factor, an antigen, a monoclonal antibody, somatostatin, adrenocorticotropin, gonadotropin releasing hormone, oxytocin, vasopressin, cromolyn sodium, vancomycin, desferrioxamine, parathyroid hormone, an antimicrobial, an antifungal agent or a combination thereof.

33. The composition according to claim 32, wherein said biologically-active agent comprises human growth hormone, an interferon, insulin, heparin, low molecular weight heparin, calcitonin, erythropoietin, cromolyn sodium, parathyroid hormone, an antimicrobial or a combination thereof.

34. The composition according to claim 33, wherein said biologically-active agent comprises human growth hormone.

35. The composition according to claim 33, wherein said biologically-active agent comprises insulin.

36. The composition according to claim 33, wherein said biologically-active agent comprises heparin.

37. The composition according to claim 33, wherein said biologically-active agent comprises low molecular weight heparin.

38. The composition according to claim 33, wherein said biologically-active agent comprises calcitonin.

39. The composition according to claim 33, wherein said biologically-active agent comprises cromolyn sodium.

40. The composition according to claim 33, wherein said biologically-active agent comprises parathyroid hormone.

41. A dosage unit form comprising

(A) a pharmacological composition according to claim 20; and

(B) (i) an excipient,

(ii) a diluent

(iii) a disintegrant

(iv) a lubricant,

(v) a plasticizer

(vi) a colorant

(vii) a dosing vehicle, or

(viii) any combination thereof..

42. A dosage unit form according to claim 41, comprising a tablet, a capsule, or a liquid.

43. A dosage unit form according to claim 41, wherein said dosing vehicle is selected form the group consisting of water, 1,2-propane diol, ethanol, and any combination thereof.

44. A method for preparing a pharmacological composition, said method comprising mixing:

(A) at least one biologically-active agent;

(B) at least one carrier compound having the formula

$$2OH\text{-}Ar\text{-}CONR^{8}\text{-}R^{7}\text{-}COOH$$

wherein Ar is a substituted phenyl or naphthyl;

R^7 is selected form the group consisting of C_4 to C_{20} alkyl, C_4 to C_{20} alkenyl, phenyl, naphthyl, (C_1 to C_{10} alkyl)phenyl, (C_1 to C_{10} alkenyl)phenyl, (C_1 to C_{10} alkyl)naphthyl, (C_1 to C_{10} alkenyl) naphthyl, phenyl (C_1 to C_{10} alkyl), phenyl (C_1 to C_{10} alkenyl), naphthyl (C_1 to C_{10} alkyl) and naphthyl (C_1 to C_{10} alkenyl);

R^7 is optionally substituted with C_1 to C_4 alkyl, C_1 to C_4 alkenyl, C_1 to C_4 alkoxy, -OH, -SH and $-CO_2R^9$ or any combination thereof;

R^7 is optionally interrupted by oxygen, nitrogen, sulfur or any combination thereof;

R^8 is selected from the group consisting of hydrogen, C_1 to C_4 alkyl, C_1 to C_4 alkenyl, hydroxy, and C_1 to C_4 alkoxy; and

R^9 is hydrogen, C_1 to C_4 alkyl, or C_1 to C_4 alkenyl;

with the proviso that the compounds are not substituted with an amino group in the position alpha to the acid group; and

(C) optionally a dosing vehicle.

45. A method for administering a biologically-active agent to an animal in need of said agent, said method comprising administering orally to said animal a composition as defined in claim 20.

46. A method for administering a biologically-active agent to a mammal in need of said agent, said method comprising administering orally to said mammal a composition as defined in claim 20.

REMARKS

The present application is a continuation of U.S. Serial No. 08/820,694, which was allowed on August 7, 2001. As this continuation application has been filed before the payment of the Issue Fee, it is timely filed.

The specification has been amended to refer to related patent applications, add interleukin-II as an active agent, and to correct a grammatical error. Support for interleukin-II is found at original claims 3 and 4. Claims 1-19 have been canceled without prejudice. Claims 20-45 have been added. Support for new claims 20-45 is found at original claims 1-19 and page 20, lines 7-13, of the specification.

In a June 3, 1999 Office Action issued in the parent application, U.S. Serial No. 08/820,694, the Examiner rejected claim 1 under 35 U.S.C. §112, first paragraph, alleging that the specification "does not reasonably provide enablement for any substituted phenyl or naphthyl, where all the possible substituents are not readily determined". While applicants disagreed with the Examiner's rejection, the claims were limited to unsubstituted phenyl or naphthyl in order to expedite prosecution of the application.

Applicants have filed this application in order to pursue claims directed to carrier compounds containing a substituted phenyl or naphtyl moiety. The phrase "substituted phenyl or naphtyl" is clearly supported in the original specification for U.S. Serial No. 08/820,694 and in this application at page 17, line 6; page 18, lines 16-18; page 24, line 10-12; and claim 1.

It is believed that the claims are free from any ground for rejection over the prior art. Early passage to allowance is respectfully requested.

Respectfully submitted,

Dated: November 7, 2001

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Marked-Up Specification
New Continuation Application
(Docket No. 1946/1B861-US2)
(Accompanying November 7, 2001 Preliminary Amendment)

IN THE SPECIFICATION:

Page 1, lines 11-13:

CROSS-REFERENCE TO OTHER RELATED APPLICATIONS

The present application is a continuation of U.S. Application Serial No. 08/820,694, filed March 18, 1997, and claims the benefit under 35 U.S.C. §119 of [based upon one] U.S. Provisional Patent Application Serial No. 60/017,902, filed March 29, 1996, both of which are hereby incorporated by reference and made part of the instant disclosure. [Applicant claims the benefit of the filing dates of the aforesaid provisional application under 35 U.S.C. §119.]

Page 20, lines 5-20:

Biologically or chemically active agents include, but are not limited to, pesticides, pharmacological agents, and therapeutic agents. For example, biologically or chemically active agents suitable for use in the present invention include, but are not limited to, peptides, and particularly small peptides; hormones, and particularly hormones which by themselves do not or only a fraction of the administered dose passes through the gastro-intestinal mucosa and/or are susceptible to chemical cleavage by acids and enzymes in the gastro-intestinal tract; polysaccharides, and particularly mixtures of muco-polysaccharides; carbohydrates; lipids; or any combination thereof. Further examples include, but are not limited to, human growth hormones; bovine growth hormones;

growth releasing hormones; interferons; interleukin-1; interleukin-II; insulin; heparin, and particularly low molecular weight heparin; calcitonin; erythropoietin; atrial naturetic factor; antigens; monoclonal antibodies; somatostatin; adrenocorticotropin, gonadotropin releasing hormone; oxytocin; vasopressin; cromolyn sodium (sodium or disodium chromoglycate); vancomycin; desferrioxamine (DFO); parathyroid hormone; anti-microbials, including, but not limited to anti-fungal agents; or any combination thereof.

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